REMARKS

Claims 1, 2, 28-33, 45-52, 54, 55, 57-59, 61-64, 69-74, 86-93, 95, 96, 98-100 and 102 were pending in the application as examined. Claims 34-44, 53, 56, 58, 59, 75-85, 94, 97, 99 and 100 were withdrawn from consideration in a previous Office Action. Claims 58, 59, 99 and 100 were recombined with the elected group in the pending Office Action. Claims 1, 2, 28-33, 45-57, 61-64, 72-74, 86-98 and 102 stand rejected under 35 U.S.C. § 102, first paragraph, for lack of written description and/or lack of enablement. Applicant has amended claims 1, 29, 31-33, 45, 49, 57, 70, 72-74, 86, 90 and 98, and has canceled claims 28, 50-56, 61, 91-97 and 102. Claims 2, 30, 46-48, 58-59, 62-64, 71, 87-89 and 99-100 remain unchanged. Therefore, claims 1, 2, 29-33, 45-49, 57-59, 62-64, 70-74, 86-90 and 98-100 are currently pending in the application. The present amendments are not in acquiescence to any position taken by the Examiner, but are made solely to expedite prosecution of the subject matter now claimed, and are thus made without disclaimer or prejudice to prosecution of claims to any subject matter which may have been lost at this time by virtue of the amendments. Applicant additionally reserves the right to re-introduce the subject matter of any of the canceled claims in continuing or divisional applications. Applicant respectfully submits that amended claims 1, 29, 31-33, 45, 49, 57, 70, 72-74, 86, 90 and 98 are fully supported by the specification and that no new matter is added through these amendments. Below we address each of the rejections stated in the Office Action as if it were applied to the newly amended claims.

Claim Amendments

Claim 1 has been amended to more particularly claim the chimeric peptides of the invention (*e.g.*, *agonist* μ opioid receptor binding moiety). Support for such language can be found throughout the specification.

Claims 29 and 70 have been amended to correct claim dependency.

Claims 31-33, 45, 49, 57, 72-74, 86, 90 and 98 have been amended to more specifically define the term "derivative". Support for this amendment can be found *inter alia* on page 10 lines 27-28 and page 11 lines 13-23.

Applicant respectfully submits that the amendments, as described above and detailed herein, do not present new matter, and Applicant thus respectfully requests consideration of these amendments in the following remarks.

Claim Objections

A. Applicant appreciates the Examiner's willingness to consider including one or more additional SEQ ID Nos. should generic claims be found allowable. The additional SEQ ID Nos. are short and few (SEQ ID Nos. 1-2 and 4-11 for μ opioid receptor binding species and SEQ ID Nos. 36 and 38-41 for SP receptor binding species). Therefore, Applicant submits that additional search of these species would not be an undue burden.

Rejections under 35 U.S.C. § 112, first paragraph - enablement

A. Claims 31-33, 45, 49, 53, 56, 57, 72-74, 86, 90, 94, 97 and 98 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and/or use the invention. Specifically, the Examiner has rejected the above-listed claims because they recite "**derivatives**", and argues that the meaning of the term in not clear enough to enable one skilled in the art to practice the invention.

Claims 53, 56, 94 and 97 have been canceled. Therefore, the rejection is now moot with respect to these claims. Claims 31-33, 45, 49, 57, 72-74, 86, 90 and 98, as amended, include language defining the scope of the term "derivative". Specifically, currently amended claims 31-33, 45, 49, 57, 72-74, 86, 90 and 98 recite that a [peptide] *derivative is obtained by alteration of the [peptide] amino acid sequence ... by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a μ opioid/Substance P receptor agonist.* The level of skill in the art of peptide chemistry was quite high at the time the invention was made. Applicant asserts that methods for altering peptide amino acid sequences by substituting, adding or deleting amino acid residues were well known at the time of invention. In addition, structure-activity studies revealing neuropeptide structure characteristics for maintaining functionality (*e.g.*, opioid and/or SP receptor binding properties) were available at the time the invention was made. See for example, Lipkowski *et al.*,

"Neuropeptides: Peptide and Nonpeptide Analogs" in *Peptides: Synthesis, Structures and Applications*, B, Gutte, ed., Academic Press, 1995, pp. 287-320, and references cited therein. A copy of this article was included with the Response to Office Action filed October 7, 2002. Furthermore, methods for assaying compounds for μ opioid receptor or Substance P receptor agonist activity were known at the time the invention was made. Thus, Applicant submits that a person of ordinary skill in the art, armed with the teachings of the present invention and the knowledge available in the art at the time the invention was made, would not be at a loss and would know how to make chimeric peptides capable of inducing analgesia from agonits μ opioid receptor binding moieties and agonist SP receptor binding moieties, or derivatives and/or fragments thereof, without undue experimentation.

B. Claims 1, 2, 28, 29-33, 45-57, 61-64, 86-98 and 102 are newly rejected under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner argues that while the specification is enabling for the claimed chimeras wherein the μ opioid receptor binding moiety is an "**agonist**", it does not reasonably provide enablement for chimeras in which the μ opioid receptor binding moiety is other than agonist.

Claims 28, 50-56, 61, 91-97 and 102 have been canceled. Therefore, the rejection is now moot with respect to these claims. Claim 1, as amended, is directed to a chimeric peptide comprising *an agonist* μ opioid receptor binding moiety at its N-terminus and an agonist Substance P receptor binding moiety at its C-terminus. As the Examiner acknowledged in the pending Office Action, the specification reasonably provides enablement for the claimed chimeras where the μ opioid receptor binding moiety is an agonist. Therefore, claims 1, 2, 29-33, 45-49, 62-64, 86-90 and 102 meet the enablement requirement.

In summary, Applicant respectfully submits that the specification provides sufficient guidance for one of ordinary skill in the art to make and use the invention, as presently claimed, without undue experimentation. Therefore, Applicant respectfully requests that the stated rejection for lack of enablement be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph – written description

A. Claims 31-33, 45, 49, 53, 56, 57, 72-74, 86, 90, 94, 97 and 98 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner has rejected the above-listed claims because they recite "**derivatives**".

Claims 53, 56, 94 and 97 have been canceled. Therefore, the rejection is now moot with respect to these claims. As discussed above, claims 31-33, 45, 49, 57, 72-74, 86, 90 and 98, as amended, include language defining the scope of the term "derivative". Specifically, currently amended claims 31-33, 45, 49, 57, 72-74, 86, 90 and 98 recite that a [peptide] *derivative is obtained by alteration of the [peptide] amino acid sequence ... by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a μ opioid/Substance P receptor agonist.* Applicant asserts that claims 31-33, 45, 49, 57, 72-74, 86, 90 and 98, and claims dependent thereof, are perfectly clear to one of ordinary skill in the art in view of the amendment and the specification, and meet the written description requirement.

B. Claims 1, 2, 28, 29-33, 45-57, 61-64, 86-98 and 102 are newly rejected under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner argues that Applicant provides no written description for opioid moieties other than agonists which can be combined with SP moieties to produce chimera.

Claims 28, 50-56, 61, 91-97 and 102 have been canceled. Therefore, the rejection is now moot with respect to these claims. Claim 1, as amended, is directed to a chimeric peptide comprising *an agonist* μ opioid receptor binding moiety at its N-terminus and an agonist Substance P receptor binding moiety at its C-terminus. As the Examiner acknowledged in the pending Office Action, the specification provides sufficient written description of agonist μ opioid receptor binding moieties that can be used in the practice of the invention. Specifically, the specification provides ample written description of what agonist μ opioid or agonist Substance P receptor binding moieties might be used to make the claimed chimera, how to make

chimeras and how to establish that the chimeras are analgesic, which is all that is required to practice the present invention. Therefore, the written description requirement with respect to claim 1, and dependent claims 2, 29-33, 45-49, 57, 62-64 and 86-90 is met.

In view of the foregoing Remarks, Applicant respectfully submits that, as required under 35 U.C.C. § 112, first paragraph, the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicant was in possession of the invention as now claimed, and thus respectfully requests that the rejection under 35 U.C.C. § 112, first paragraph (written description) be withdrawn.

Information Disclosure:

In an effort to complete the list of citations that will be printed on the patent, Applicant has provided herewith a copy of PTO-1449 and an information disclosure statement citing a journal article, a copy of which was included in Applicant's Response to Office Action filed October 7, 2002.

In view of the foregoing Amendments and Remarks, Applicant respectfully submits that the present case is now in condition for allowance; a Notice to that effect is hereby requested. Applicant would like to thank the Examiner for careful review and consideration of this case and if the Examiner believes that a telephone interview would be of assistance in advancing the prosecution of this application, the Examiner is invited to telephone the undersigned (617) 248-5150.

A check for $180.00 covering the fee set forth in 37 C.F.R § 1,17(p) is included herewith. If additional fee(s) is(are) required, please charge or credit any overpayment to our Deposit Account No.: 03-1721.

Respectfully submitted,

Date: June 18, 2003

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner For Patents, P.O. Box 1450, Alexandria, VA 22313
on June 18, 2003
Kathy Hart Gagnon

- APPENDIX A -

Claims as Pending After Entrance of the Present Amendment

1. (Thrice amended) A chimeric peptide comprising an agonist μ opioid receptor binding moiety at its N-terminus and an agonist Substance P receptor binding moiety at its C-terminus, wherein said peptide induces analgesia.

2. (Original) The peptide of claim 1, wherein said peptide induces analgesia when administered to a mammal.

Claims 3-28 (Canceled)

29 (Once amended) The peptide of claim 1 wherein the N-terminal amino acid residue of said opioid receptor binding moiety is a free amine.

30 (Once added) The peptide of claim 29 wherein the N-terminal amino acid residue of said opioid receptor binding moiety is Tyr.

31 (Once amended) The peptide of claim 30 wherein said opioid receptor binding moiety is a peptide having any one of SEQ ID Nos: 1-11, or an N-terminal fragment or N-terminal derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of any one of SEQ ID Nos: 1-11 by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a μ opioid receptor agonist.

32 (Twice amended) The peptide of claim 30 wherein said opioid receptor binding moiety is endomorphin 1, endomorphin 2, an N-terminal fragment, or an N-terminal derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of endomorphin 1 or endomorphin 2 by substitution, addition or deletion of one or more

amino acids, whereby the derivative is at least 4 amino acid residues long and is a μ opioid receptor agonist.

33 (Twice amended) The peptide of claim 32 wherein said opioid receptor binding moiety is a peptide having SEQ ID No: 2 or 3, or an N-terminal fragment or N-terminal derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of SEQ ID No: 2 or 3 by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a μ opioid receptor agonist.

Claims 34-44 (Canceled)

45. (Twice amended) The peptide of claim 1, wherein said agonist Substance P receptor binding moiety comprises Substance P, a C-terminal Substance P fragment, or a C-terminal Substance P derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of Substance P by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a Substance P receptor agonist.

46. (Once amended) The peptide of claim 1, wherein the –COOH moiety of the C-terminal amino acid residue of said Substance P receptor binding moiety is protected.

47. (Once added) The peptide of claim 46 wherein the –COOH moiety of the C-terminal amino acid residue of said Substance P receptor binding moiety is amidated.

48. (Once added) The peptide of claim 47 wherein the C-terminal amino acid residue of said Substance P receptor binding moiety is Met-NH_2.

49. (Twice amended) The peptide of claim 48 wherein said Substance P receptor binding moiety is a peptide having any one of SEQ ID Nos: 21, 36 and 38-41, or a C-terminal

fragment or C-terminal derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of any one of SEQ ID Nos: 21, 36 and 38-41 by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a Substance P receptor agonist.

Claims 50-56 (Canceled)

57. (Twice amended) The peptide of claim 1 wherein

the opioid receptor binding moiety is endomorphin 1, endomorphin 2, or an N-terminal fragment or N-terminal derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of endomorphin 1 or endomorphin 2 by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a μ opioid receptor agonist; and

the Substance P receptor binding moiety is Substance P, or a C-terminal fragment or a C-terminal Substance P derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of Substance P by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a Substance P receptor agonist.

58. (Once added) The chimeric peptide of claim 1 wherein the peptide has SEQ ID No: 42.

59. (Once added) The chimeric peptide of claim 1 wherein the peptide has SEQ ID No: 43.

Claims 60-61 (Canceled)

Claim 65 (Once added) A pharmaceutical composition comprising the peptide of claim 1 and a pharmaceutically acceptable diluent.

Claim 66 (Once added) The pharmaceutical composition of claim 62, further comprising an adjuvant.

Claim 67 (Once amended) The pharmaceutical composition of claim 62, wherein said peptide induces analgesia when administered to a mammal.

Claims 65-68 (Canceled)

69. (Twice amended) The pharmaceutical composition of claim 62 wherein the N-terminal amino acid residue of said opioid receptor binding moiety is a free amine.

70. (Once amended) The pharmaceutical composition of claim 70 wherein the N-terminal amino acid residue of said opioid receptor binding moiety is Tyr.

71. (Twice amended) The pharmaceutical composition of claim 71 wherein said opioid receptor binding moiety is a peptide having any one of SEQ ID Nos: 1-11, or an N-terminal fragment or N-terminal derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of any one of SEQ ID Nos: 1-11 by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a μ opioid receptor agonist.

72. (Twice amended) The pharmaceutical composition of claim 71 wherein said opioid receptor binding moiety is endomorphin 1, endomorphin 2, an N-terminal fragment, or an N-terminal derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of endomorphin 1 or endomorphin 2 by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a μ opioid receptor agonist.

73. (Twice amended) The pharmaceutical composition of claim 73 wherein said opioid receptor binding moiety is a peptide having SEQ ID No: 2 or 3, or an N-terminal fragment or N-terminal derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of SEQ ID No: 2 or 3 by substitution, addition or

deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a μ opioid receptor agonist.

Claims 75-85 (Canceled)

86. (Twice amended) The pharmaceutical composition of claim 62, wherein said agonist Substance P receptor binding moiety comprises Substance P, a C-terminal Substance P fragment, or a C-terminal Substance P derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of Substance P by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a Substance P receptor agonist.

87. (Once amended) The pharmaceutical composition of claim 62, wherein the –COOH moiety of the C-terminal amino acid residue of said Substance P receptor binding moiety is protected.

88. (Once amended) The pharmaceutical composition of claim 87 wherein the –COOH moiety of the C-terminal amino acid residue of said Substance P receptor binding moiety is amidated.

89. (Once amended) The pharmaceutical composition of claim 88 wherein the C-terminal amino acid residue of said Substance P receptor binding moiety is Met-NH_2.

90. (Twice amended) The pharmaceutical composition of claim 89 wherein said Substance P receptor binding moiety is a peptide having any one of SEQ ID Nos: 21, 36 and 38-41, or a C-terminal fragment or C-terminal derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of any one of SEQ ID Nos: 21, 36 and 38-41 by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a Substance P receptor agonist.

Claims 91-97 (Canceled)

98. The pharmaceutical composition of claim 62 wherein

the opioid receptor binding moiety is endomorphin 1, endomorphin 2, or an N-terminal fragment or N-terminal derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of endomorphin 1 or endomorphin 2 by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a μ opioid receptor agonist; and

the Substance P receptor binding moiety is Substance P, or a C-terminal fragment or a C-terminal Substance P derivative thereof; wherein the derivative is obtained by alteration of the amino acid sequence of Substance P by substitution, addition or deletion of one or more amino acids, whereby the derivative is at least 4 amino acid residues long and is a Substance P receptor agonist.

99. (Once amended) The pharmaceutical composition of claim 62 wherein the peptide has SEQ ID No: 42.

100. (Once amended) The pharmaceutical composition of claim 62 wherein the peptide has SEQ ID No: 43.

Claims 101-102 (Canceled)